A comparative study of chondroitin sulfate and heparan sulfate for directing three-dimensional chondrogenesis of mesenchymal stem cells.

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Public Summary:
Mesenchymal stem cells (MSCs) hold great promise for cartilage repair given their relative abundance, ease of isolation, and chondrogenic potential. To enhance MSC chondrogenesis, extracellular matrix components can be incorporated into three-dimensional (3D) scaffolds as an artificial cell niche. Chondroitin sulfate (CS)-containing hydrogels have been shown to support 3D chondrogenesis, but the effects of varying CS concentration and hydrogel stiffness on 3D MSC chondrogenesis remains elusive. Heparan sulfate (HS) is commonly used as a growth factor reservoir due to its ability to sequester growth factors; however, how it compares to CS in supporting 3D MSC chondrogenesis remains unknown. We fabricated photocrosslinkable hydrogels containing physiologically relevant concentrations (0-10%) of CS or HS with two stiffnesses (~7.5 kPa and ~ 36 kPa) as a 3D niche for MSC chondrogenesis. CS is a more potent factor in enhancing MSC chondrogenesis, especially in soft hydrogels (~ 7.5 kPa). A moderate dosage of CS (5%) led to the highest amount of neocartilage deposition. Stiff hydrogels (~ 36 kPa) generally inhibited neocartilage formation regardless of the biochemical cues. CONCLUSIONS: Taken together, the results from this study demonstrated that CS-containing hydrogels at low mechanical stiffness can provide a promising scaffold for enhancing MSC-based cartilage tissue regeneration.

Scientific Abstract:
BACKGROUND: Mesenchymal stem cells (MSCs) hold great promise for cartilage repair given their relative abundance, ease of isolation, and chondrogenic potential. To enhance MSC chondrogenesis, extracellular matrix components can be incorporated into three-dimensional (3D) scaffolds as an artificial cell niche. Chondroitin sulfate (CS)-containing hydrogels have been shown to support 3D chondrogenesis, but the effects of varying CS concentration and hydrogel stiffness on 3D MSC chondrogenesis remains elusive. Heparan sulfate (HS) is commonly used as a growth factor reservoir due to its ability to sequester growth factors; however, how it compares to CS in supporting 3D MSC chondrogenesis remains unknown. METHODS: We fabricated photocrosslinkable hydrogels containing physiologically relevant concentrations (0-10%) of CS or HS with two stiffnesses (~7.5 kPa and ~ 36 kPa) as a 3D niche for MSC chondrogenesis. RESULTS: CS is a more potent factor in enhancing MSC chondrogenesis, especially in soft hydrogels (~ 7.5 kPa). A moderate dosage of CS (5%) led to the highest amount of neocartilage deposition. Stiff hydrogels (~ 36 kPa) generally inhibited neocartilage formation regardless of the biochemical cues. CONCLUSIONS: Taken together, the results from this study demonstrated that CS-containing hydrogels at low mechanical stiffness can provide a promising scaffold for enhancing MSC-based cartilage tissue regeneration.